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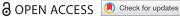
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Searching for effective components of cognitive rehabilitation for children and adolescents with acquired brain injury: A systematic review

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ABSTRACT

Aim. Cognitive rehabilitation is of interest after paediatric acquired brain injury (ABI). The present systematic review examined studies investigating cognitive rehabilitation interventions for children with ABI, while focusing on identifying effective components. Components were categorized as (1) metacognition and/or strategy use, (2) (computerized) drill-based exercises, and (3) external aids. Methods. The databases PubMed (including MEDLINE), PsycInfo, and CINAHL were searched until 22nd June 2017. Additionally, studies were identified through cross-referencing and by consulting experts in the field. Results. A total of 20 articles describing 19 studies were included. Metacognition/strategy use trainings (five studies) mainly improved psychosocial functioning. Drill-based interventions (six studies) improved performance on tasks similar to training tasks. Interventions combining these two components (six studies) benefited cognitive and psychosocial functioning. External aids (two studies) improved everyday memory. No studies combined external aids with drill-based interventions or all three components. Conclusion. Available evidence suggests that multi-component rehabilitation, e.g. combining metacognition/strategy use and drill-based training is most promising, as it can lead to improvements in both cognitive and psychosocial functioning of children with ABI. Intervention setting and duration may play a role. Conclusions remain tentative due to small sample sizes of included studies heterogeneity regarding outcome measures, intervention and therapist variables, and patient characteristics.

ARTICLE HISTORY

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KEYWORDS

Interventions; cognition; cognitive rehabilitation; brain injury; paediatric

Acquired brain injury (ABI) is damage to the brain that occurred after birth, but is not related to congenital diseases or neurodegenerative disorders (1). Aetiologies include traumatic brain injury (TBI), infections (e.g. encephalitis or meningitis), brain tumours, stroke, and hypoxia (2). In the Netherlands, each year approximately 19 000 children and adolescents are diagnosed with ABI (3). Incidence rates in other countries such as Australia and the UK seem to be even higher (4,5). Children and adolescents who are diagnosed with ABI frequently report post-injury (i.e. directly after injury as well as several months to years later) problems with cognitive functions, such as attention, memory, and executive functions (6–9). In turn, these cognitive difficulties may negatively impact a patient's psychosocial functioning including social participation, family functioning, and quality of life (10-13). Improving cognitive functioning after paediatric ABI is therefore believed to be essential for neurocognitive as well as psychosocial rehabilitation and recovery.

Over the last decade, multiple reviews have contributed to collecting and describing available effect studies into cognitive rehabilitation after paediatric ABI (2,14-18). Cognitive rehabilitation is defined as a systematic intervention directed at restoring impaired cognitive abilities or compensating for the impact of present difficulties (19). The most recent review into this topic searched for articles published before May 2013 (17). Since then, the literature in this rapidly evolving field of investigation, especially in training with computer games, has been growing, and an update of the literature is warranted. Therefore, the present review aimed to provide an up-to-date overview of studies into the effectiveness of cognitive rehabilitation for children with ABI.

In previous reviews, it has been pointed out that there is a need for explicit identification of the active components in effective cognitive rehabilitation interventions (2,15,16,18). Categorizing cognitive rehabilitation interventions based on their different components might advance our knowledge on what intervention components are most effective in improving cognitive functioning of children and adolescents with ABI. Furthermore, it enables researchers and clinicians to compare different interventions and to select the most appropriate intervention for the cognitive problems at hand. In the present systematic review, we explicitly focus on intervention

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components when examining the available literature on intervention effectiveness in improving cognitive functions in children and adolescents with ABI. More specifically, we aimed to delineate the effects of different types of interventions to identify their effective components.

For the purpose of this review, three main intervention components are distinguished: (1) metacognition and/or strategy use, (2) (computerized) drill-based exercises, and (3) external aids. Metacognition training is directed at teaching participants to 'think about their thinking' and provides general instructions, for example 'What is the best way to approach a (i.e. any) task?'. Strategy use can be defined as instructions to approach a specific task, for example, 'How can you best remember this list of words?'. Drill-based training is based on repeated practice of simple exercises, either on the computer or on paper, mostly targeting one particular cognitive function, such as working memory. Sometimes these exercises are placed in a game-like context, like adventurous journeys and treasure hunts. Lastly, external aids, such as diaries and pagers provide children and adolescents with ABI with external support (e.g. notes and reminders) to compensate for cognitive difficulties and to aid daily life functioning. The different intervention components are used either alone or combined, for example, an intervention may consist only of drill-based exercises or can be a combined drill-based practice with metacognitive training.

The present systematic review focused on interventions targeting cognitive functioning (e.g. attention, memory, and/ or executive functions), either on the level of functions or on the level of activities. For example, memory on the level of functions can refer to the ability to remember certain stimuli in a memory task, while memory on the level of activities can mean the ability to remember important daily tasks. Furthermore, possible generalizable effects to other areas of functioning (e.g. social participation, family functioning, and quality of life) were investigated. We included studies with a wide range of clinical trial designs (i.e. not only randomized controlled trials), since high-quality non-randomized controlled studies have previously been found to produce similar treatment effect sizes as randomized controlled trials (20,21). Quality of all included studies and their risk of bias will be explicitly evaluated in the following sections.

Methods

A systematic review was designed and reported in accordance with the PRISMA (preferred reporting items for systematic reviews and meta-analyses) statement (22,23). No review protocol was published.

Eligibility criteria

Studies were included when they met the following criteria: (1) a non-pharmacological intervention directed at improving cognitive functioning (i.e. attention, executive functions, information processing, language, memory, and/or perception) was investigated.; (2) cognitive functioning was assessed on the level of functions (e.g. with cognitive tests) and/or on

the level of activities (e.g. with questionnaires or interviews about daily life cognitive functioning); (3) participants were diagnosed with ABI (i.e. TBI, brain tumour, brain infections, stroke, or hypoxia). If the study included patients with other diseases than ABI that affect the central nervous system (CNS) and/or cognitive functioning (e.g. acute lymphoblastic leukaemia), data for children and adolescents with ABI and data for children with other diseases had to be presented separately or at least 50% of the participants had to be diagnosed with ABI, to be included; (4) the sample consisted of children and adolescents (i.e. age <19 years). If the sample also included adults, the study was only included if data for children and adolescents and data for adults were presented separately or at least 50% of the participants were children or adolescents; (5) results were statistically analysed whereby outcomes of the intervention group were compared either to outcomes of another intervention group or to pre-intervention functioning (i.e. no case studies or single-case designs); (6) the study was an empirical study; (7) the study was published in a peerreviewed journal article.

Information sources

The search was conducted in PubMed including MEDLINE (1966-present), PsycInfo (1967-present), and CINAHL (1982-present) electronic databases to identify studies published in English, Dutch, or German. The initial search was carried out on 28th May 2015. For all three databases, the authors performing the search (CR and SR) created e-mail alerts to be kept up to date if a new article that met the search criteria was added to the database. Therefore, the current systematic review encompasses articles that were included in the above described databases before 22nd June 2017. In addition to the database search, the reference lists of the included full-text articles and of relevant review articles and meta-analyses known to the authors were examined, and the expert network of the authors was consulted for articles relevant for the present review.

Search

Search terms were formulated according to three categories: ABI, intervention, and cognition. With the aim to investigate effectiveness of cognitive rehabilitation in a paediatric ABI population, terms within a category were combined with OR, while the three categories were combined with AND (i.e. brain injury OR head injury [...] AND intervention OR training [...] AND cognition OR cognitive [...]). For the search, all individual keywords were separately entered in the MeSH or Thesaurus databases to find the appropriate index terms used in the electronic databases. Supplementary material 1 displays the search terms as well as the full electronic search for the PubMed database including all MeSH terms. The searches were employed without date restriction. Results were limited to (controlled) clinical trials and empirical studies with a paediatric population.



Study selection

Two of the authors (CR and SR) independently reviewed the articles at each stage of the literature search (i.e. screening titles, screening abstracts, and reading full-texts) to determine inclusion eligibility. In case of doubt, two other authors (PH and CH) were consulted.

Data collection process and data items

Data were extracted by one author (CR). The following information was collected whenever available: (1) study characteristics, i.e. authors and design; (2) patient characteristics, i.e. sample size, diagnosis, time post-injury, age, baseline level of cognitive functioning; (3) intervention characteristics, i.e. type of intervention, setting, duration, and frequency; and (4) outcome measures, i.e. cognitive outcomes on the level of functions (i.e. with cognitive testing), cognitive outcomes on the level of activities (i.e. questionnaires or interviews about daily life cognitive functioning, goal setting regarding cognition), and other outcomes (e.g. psychosocial or academic).

Risk of bias within and across studies

Risk bias within the included studies was assessed by two authors (CR and SR) with the Quality Assessment Tool for Quantitative Studies (Effective Public Health Practice Project) (24). This is one of the methods for risk bias assessment recommended by the Consolidated Standards of Reporting Trials (25). The method includes ratings of eight different domains (i.e. selection bias, study design, confounders, blinding, data collection methods, withdrawals and drop-outs, intervention integrity, and analyses) to judge the extent of the presence of bias. A study can be assessed as 'strong', 'moderate', or 'weak', where a 'strong' rating equals a low risk of bias. The tool is applicable to randomized trials as well as non-randomized studies and quasi-experimental designs. Furthermore, it has shown excellent inter-rater agreement for the final rating and fair agreement for individual domains (24) and was previously found to be one of the best quality assessment tools and useful in systematic reviews (26).

Risk of bias across studies was considered, but could not be addressed statistically, due to the large variation in study designs and outcome measures of the included studies. The authors of the present review considered it unlikely that there were many studies unpublished due to non-significant results since investigations into cognitive rehabilitation after paediatric ABI are still rare and the present review demonstrated that many of the published studies also showed non-significant effects.

Results

Study selection

Details concerning the study selection are illustrated in a flow diagram in Figure 1. A total of 1911 articles were identified during the first search of the electronic databases on 28th May 2015. After duplicates were removed, titles of 1812 articles were screened. Based on the titles, 1668 articles were excluded. Reviewing abstracts of the remaining 144 articles left 67 full texts to be examined in more detail. A total of 11 examined full texts met all eligibility criteria. The authors specifically want to remark on the exclusion of studies into familycentred interventions (see for example (27-31)) and on a peer-supported metacognition intervention (32). While these studies examine cognitive functioning as one of their primary outcome measures, the interventions themselves were mainly focused on finding the best intervention context (i.e. familycentred or clinician delivered) (27), or were directed at family problem-solving and communication (28-31) or cooperative learning and social mediation (32). While these studies give a good indication that family and/or peer involvement can be beneficial for rehabilitation after paediatric ABI, it would not be clear whether an effect of the intervention would have been the result of the intervention itself or of the system involved. Therefore, the authors decided to exclude these studies from the present review.

E-mail alerts from the searched database until 22nd June 2017 revealed two additional articles (33,34). An inquiry in the expert network of the authors yielded four more articles that met inclusion criteria (35-38). Finally, another three articles (39-41) that met the eligibility criteria were found in reference lists of the previously included articles. In total, 20 articles were included. Two of these articles were combined in further description, since one of them (42) reported follow-up data from the study described in the other one (43), making a total of 19 included studies.

Risk of bias within studies

Five of the included 19 studies were randomized controlled trials, of which one was analysed as a pre-/post-test trial. Five of the other studies used a (non-randomized) control group, the other nine studies were uncontrolled trials. Results based on studies not designed as randomized controlled trials should be interpreted with caution: the absence of a control group makes it impossible to disentangle intervention effects from confounding due to time or retesting effects and regression to the mean. Furthermore, the absence of a thorough randomization procedure might lead to selection bias over the groups. Ratings of risk bias within studies are displayed per study in Tables 1-4.

Syntheses of results

Below, we will describe the main findings for each of the intervention types and combination of types that we have encountered in the included studies (i.e. metacognition and/ or strategy use, drill-based exercises, metacognition/strategy use combined with drill-based exercises, external aids, and metacognition/strategy use combined with external aids). No investigated intervention combined drill-based exercises with external aids, or made use of a combination of all three interventions components. An overview per study is presented in Tables 1-4. All results will be described while considering the great heterogeneity across studies in terms of age of participants, types and severity of brain injury, time post-

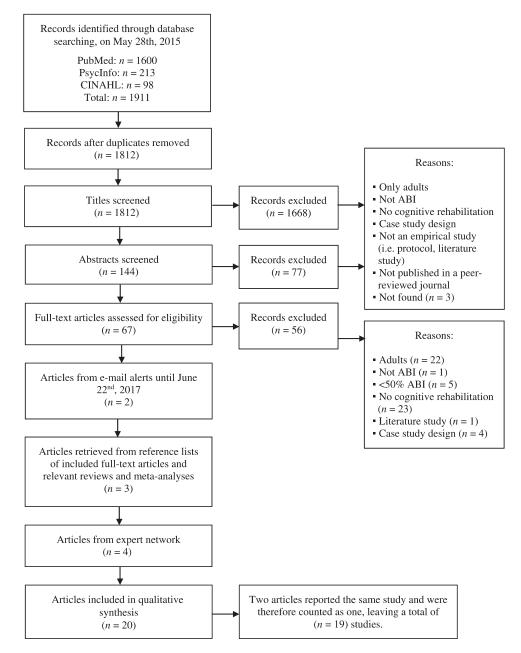


Figure 1. Flowchart for the literature search and the study selection. Adapted from "Preferred reporting items for systematic reviews and meta-analyses: the PRISMA Statement", by D. Moher, A. Liberati, J. Tetzlaff, D.G. Altman, and The PRISMA Group, 2009, PLoS Med 6(6). Copyright by the Public Library of Science.

injury, treatment setting, and intervention duration and frequency.

When synthesizing the results, it was noted that occasionally, the same outcome measure was categorized as measuring different aspects of cognitive and/or psychosocial functioning by different authors. For example, the Digit Span task consists of two parts: recalling a string of digits in the same order as presented (Digit Span Forward) and recalling these digits in the reversed order (Digit Span Backward). Moreover, these two task parts are often grouped together in a Digit Span Total Score or a larger composite score. This Digit Span Total Score (48,49) and/or composite scores including this test were used as a measure of working memory by some studies (34,35,50), while others used them

as indicators for attention (41,51) or memory (41–43). To be consistent in reporting the results for different outcome domains, the outcome measures used in the original articles were occasionally re-grouped. For example, in line with the assumption that the Digit Span Backward measures working memory and not solely attention or memory (52), the score on this test or any composite score including this test was categorized as a measure of working memory.

Metacognition and/or strategy use

Six cognitive rehabilitation interventions, examined in five different studies, were based on metacognition and/or strategy use. One study was a randomized controlled trial and one was

Table 1. Overview of studies into interventions based on metacognition/strategy use.

Study characteristics		_	Intervention character	Main findings ^c	
Authors, quality ^a	Design and measures	Patient characteristics	Intervention	Setting, duration and frequency ^b	I: Cognition on level of functions II: Cognition on level of activities III: Psychosocial and academic outcomes
Chan & Fong, 2011 (44) Strong	Quasi- experimental, matched pairs controlled pre-/ post-test design. Pre-post	n = 32 (E:16, C:16) Injury: 21 moderate to severe TBI, 6 BT, 5 AVM, >3 y post-injury Age: 7–16 y • Objectified problem-solving difficulties.	Problem-solving skills training with metacognitive principles; pen and paper exercises, group games and discussions, role play, self-evaluation. Control intervention: Attending school.	5–6 children, 2 therapists. Parents receive strategy instruction. Duration/frequency: Scheduled:7 w, 2 sessions/w, 3 h/ session	I: + Metacognition, intellectual functioning and social problem-solving. II: + Parent-reported executive functioning III: + Child- and parent-reported goal-directed functional behaviour
Cook et al., 2014 (35) Moderate	Single-blind (pseudo) randomized controlled pilot design. Pre–post	n = 20 (E1:10, E2:10) Injury: Mild to severe TBI, 0.6– 13.1 y post- injury • Objectified gist reasoning difficulties.	E1 = SMART: top-down gist reasoning training, strategy-based pen and paper tasks and individual exercises with personal examples. E2 = Fact-based memory training: Bottom-up training with pen and paper tasks and school work tasks.	1:1 with speech- language clinician at home, at the school library or at the community centre. <i>Duration/frequency:</i> <i>Scheduled:</i> 1 m, 8 sessions, 45 min/session	I: = intellectual functioning; + only SMART group: abstracting meaning from complex information (some parameters), verbal working memory, inhibition II: + only fact-based memory training group: parent-reported everyday executive functioning III: NA
Light et al., 1987 (40) Weak	Quasi- experimental controlled pre-/ post-test design Pre–post	n = 21(E:15, C:6) Injury: TBI, ±2.5– 3.5 y post-injury' Age:4–10 y	NEP: Programme for attention, memory, behavioural/self-control and problem solving. Pen and paper exercises, cognitive strategies, and counselling for problems at home. Control group: Passive.	Setting: 1:1 tutoring at school and at home by volunteer Duration/frequency: Scheduled: 6 m, 2 sessions/w at school + 1 session/w at home Actual:3–7 m (M: 21 w), 19–68 hours (M: 39.7, SD 14.2)	I: = intellectual functioning, spatial memory, picture memory, attention, receptive and expressive vocabulary, verbal fluency, visual motor integration II: NA III: + adaptive behaviour in area of communication; = Academic achievement tests, parent reports of child behaviour, daily living skills, socialization, maladaptive behaviour
Missiuna et al., 2011 (53) Weak	Quasi- experimental pre-/post-test design Pre-post – 4 m	n = 6 Injury: mild to moderate TBI, 6–19 m post- injury Age: 6–15 y • Unable to fully participate in all school settings.	CO-OP: problem-solving training based on the Goal-Plan-Do-Check strategy, linked to daily life situations.	Setting: 1:1 with occupational therapist. Duration/frequency: Scheduled: 10 w, 1session/w, 1 h/session	I: NA II: + individually selected functional task performance, performance satisfaction III: + adaptive behaviour in communication, daily living skills, social skills (All improvements maintained to 4 m follow-up)
	Quasi- experimental pre-/post-test design Pre–post	n = 12 Injury: 9 BT, 2 Leukaemia, 1 CNS Histiocytosis, 2–12 y, post- injury Age: 7–19 y • Objectified attention and memory problems.	Five-component programme: (1) problem- solving, (2) study skills, and metacognition, (3) information processing strategies, (4) compensatory techniques for academic performance, and (5) collaborate with parent to reinforce strategy use at home.	Setting: 1:1 with therapist. Duration/frequency: Scheduled:3 m, 15 w, 1 session/w, 60–90 min/ session Actual: 6 m, 7–15 sessions	I: + quality of writing; = attention, verbal working memory, verbal learning skills, writing comprehension II: = attention behaviour III: + social behaviour with respect to cooperation, assertion, empathy and self-control; = externalizing and internalizing behaviours

^aBased on the Quality Assessment Tool for Quantitative Studies (Effective Public Health Practice Project). ^b Whenever possible, scheduled as well as actual training duration and frequency are displayed. C+: improvement, = : no change, -: deterioration, NA: 'not assessed'. Abbreviations: E = experimental group, C = control group, y = year(s), m = month(s), w = week(s), h = hour(s), min = minutes, M = mean, SD = standard deviation. Abbreviations injury: AVM = Arteriovenous malformation, BT = brain tumour, CNS = central nervous system, TBI = traumatic brain injury. Abbreviations interventions: CO-OP = Cognitive Orientation to Daily Occupational Performance, NEP = Neuro-Cognitive Education Project, SMART = Strategic Memory Advanced Reasoning Training.

a controlled clinical trial, both using an active control group. The other three studies were quasi-experimental pre-/post-test designs, of which one (40) used a passive control group (i.e. a control group that received no alternative treatment). Samples ranged from n = 6 to n = 32, including patients with mild to severe TBI, brain tumours, and other forms of cancer not located in but still affecting the brain. Interventions were provided in a 1:1 patient-therapist setting, except for one small-group (i.e. five to six children per two therapists)

metacognition training. Intervention duration ranged from 6 to 42 hours over 7 weeks to 10 months.

Metacognition and/or strategy use seemed especially powerful in improving areas of functioning other than cognition. Three of five studies investigated this and found improvements in social behaviour and adaptive communication behaviour. Neither cognitive functioning on the level of functions nor cognitive functioning on the level of activities were found to change consistently, although it seems that the



Table 2. Overview of studies into interventions based on (computerized) drill-based exercises.

Study characteristics		_	Intervention	Main findings ^c	
Authors, quality ^a	Design and measures	Patient characteristics	Intervention	Setting, duration and frequency ^b	I: Cognition on level of functions II: Cognition on level of activities III: Psychosocial and academic outcomes
de Kloet et al., 2012, (45) Moderate	Multicentre quasi- experimental pre-/post-test design Pre-post	n = 50 Injury: 27 TBI, 23 nTBI, 0–2 y post-injury Age: 6–29 y	Nintendo Wii TM: a selection of computerized games directed at information processing, fine and gross motor skills, communication, self-confidence, social participation and/or daily physical activity.	Setting: At home training, two initial 1 h training sessions with a clinician at participating centre. Duration/frequency: Scheduled:12 w, 2 days/w, 20 min/day	I: + alertness, attentional flexibility, visuospatial working memory, motor tracking improved (all on some parameters) II: NA III: + time spent on physical activities, goal achievement rating, parent-reported quality of life regarding school aspects, participation with respect to recreational diversity and physical frequency
Eve et al., 2016 (34) Moderate	Quasi- experimental pre-/post-test design Pre-post – 12 m	n = 7 Injury: Arterial ischemic stroke, 4–10 y post- injury Age: 10–16 y • Average to below-average working memory skills.	Cogmed TM : computerized tasks targeting verbal and visuospatial working memory.	Setting: Individual home training, parental supervision. Weekly phone calls with coach to promote training adherence and motivation. Reward for participants after post-test. Duration/frequency: Scheduled: 5–7 w, 25 sessions, 5 sessions/w, 30–40 min/session Actual: as scheduled	I: + verbal working memory (not maintained to follow-up); = visual-spatial working memory, attention, inhibition II: NA III: = academic performance.
Hardy et al., 2011 (50) Moderate	Quasi- experimental pre-/post-test pilot design Pre-Post – 3 m	n = 9 Injury: 6 BT, 3	Captain's Log: computer training consisting of game-like exercises for attention, memory, listening skills, processing speed and self-control.	Setting: Home-based training, weekly phone calls with researcher to address problems. Earn gift cards in week 4, 8, and 12 to enhance compliance. Duration/frequency: Scheduled: 12 w, ≥50 min/w Actual: 9–53 sessions (M: 28.4), 3.7–20.8 h (M: 11.4).	I: + three of the five verbal working memory indices (two of which remained improved at a 3-month follow-up) II: + parent-reported attention between pre-test and follow-up (but not between pre-test and post-test) III: NA.
Kaldoja et al., 2015 (36) Weak	Quasi- experimental pre-/post-test design pre-post – 1.63 y	n = 8 Injury: 5 mild TBI, 3 Partial Epilepsy, ± 3.79 y post- injury Age: 9–12 y • Mild to moderate attention	FORAMEN Rehab®: Cognitive rehabilitation software training focused, sustained, and complex, and tracking.	Setting: 1:1 sessions with therapist at outpatient children's clinic. Duration/frequency: Scheduled: 6 w, 2 sessions/w, 30–50 min/session	I: + performance on some of the FORAMENRehab programme tasks (some maintained to follow-up) II: NA III: NA
Phillips et al., 2016 (37) Moderate	Randomized controlled design Pre– post – 3 m	13)	Cogmed TM : see Eve et al., 2016 <i>Control intervention</i> : non-adaptive Cogmed training (i.e. working memory span was continuously kept at a level of 3).	Setting: See Eve et al., 2016 Additions: Reminder e-mails. Reward for participants after every 5 sessions. Duration/frequency: Scheduled:5 w, 5 sessions/w, 30–40 min/session Actual: Training days/w M: 4.49 SD: 0.93. Total time training: M 10.23– 14.76 h.	l: + visual-spatial working memory (maintained to follow-up); = verbal working memory, attention, inhibition ll: NA Ill: + reading comprehension at post-test, reading accuracy at follow-up; = mathematics
Thomas- Stonell et al., 1994 (46) Weak	Randomized controlled double pre- test design Pre 1– Pre 2 (4 w)–post	n = 12 (E: 6, C: 6) Injury: TBI, 3 m- 47 post-injury Age: 12–21 y • Deficits in cognitive- communication based on assessment.	Computer-based TEACHware TM directed at word retrieval, attention, understanding abstract language, organization, and problem solving. <i>Control interventions</i> : School programmes ($n = 3$), traditional rehabilitation ($n = 3$).	1:1 with speech-language pathologist, teacher, or occupational therapist; clinician helps transfer learned skills to daily life activities. <i>Duration/frequency:</i> Scheduled: 8 w, individualized number of sessions/w (M: 2), 1 h/ session.	I: + verbal memory, word retrieval, comprehension, and problem- solving in language tasks (on some parameters), composite scores of language tests; = organization in language tasks

^a Based on the Quality Assessment Tool for Quantitative Studies (Effective Public Health Practice Project). ^b Whenever possible, scheduled as well as actual training duration and frequency are displayed. c +: improvement, = : no change, \rightarrow : deterioration, NA: 'not assessed'. *Abbreviations*: E = experimental group, C = control group, y = year(s), w = week(s), h = hour(s), min = minutes, M = mean, SD = standard deviation, Md = median.*Abbreviations injury*: ALL = acute lymphoblasticleukaemia, BT = brain tumour, TBI = traumatic brain injury, nTBI = non-TBI.

Table 3. Overview of studies into interventions combining metacognition/strategy use and (computerized) drill-based exercises

Study characteristics		_	Intervention characteristics		Main findings ^c
Authors, quality ^a	Design and measures	Patient characteristics	Intervention	Setting, duration and frequency ^b	Cognition on level of functions II: Cognition on level of activities III: Psychosocial and academic outcomes
Brett & Laatsch, 1998 (39) Moderate	Quasi- experimental pre-/post- test design Pre-post	n = 10 <i>Injury</i> :: 9 TBI, 1 Infection, 1–16y post-injury <i>Age</i> : 14.4–18.7y	Computerized exercises and interactive tasks with metacognition targeting (1) alertness, attention, concentration, (2) perception and memory, (3) problemsolving.	Setting: 1:1 or 1:2 treatment from specialized teacher ($n = 6$) or group treatment ($n = 4$). Duration/frequency: Scheduled: 20 w, 2 sessions/w, 40 min/session Actual: 18–42 sessions (md: 33.5)	I: + memory; = intellectual functioning, problem-solving abilities II: NA III: = self-esteem
Catroppa et al., 2015 (33) Moderate	Quasi- experimental pre-/post-test design <i>Measures</i> : Pre-post – 6 m	n = 10 Injury: 8 TBI, 1 Hypoxia, 1 Birth trauma, 1.6– 12.7 y post-injury Age: 8.4–13.6 y • Objectified attention and/or memory problems.	AMAT-C: Drill-based exercises and attention and memory techniques.	Setting: 30 min per day homework with parent, 1 h per week with therapist in clinic Duration/frequency: Scheduled: 18 w, 30min/d, 6d/w + 1h/w Actual: Homework complete 62–100% (M: 92)	l: + visual memory (up to 6-month follow-up); = attention, verbal memory ll: = parent-reported executive functioning lll: = (adaptive) behaviour
Galbiati et al, 2009 (47) Weak	Quasi- experimental controlled pre-/post-test design Pre – 1 y	N = 65 (E:40, C:25) Injury: Severe TBI, ±6−10 m post- injury Age: 6−18 y • Objectified attention deficits.	Computer training and table-top tasks targeting attention (i.e. selective, focused, sustained, divided, inhibition, shifting) and metacognition. Control intervention: Passive	Setting: 1:1 with therapist at the institute. Duration/frequency: Scheduled: 6 m, 4 sessions/w, 45 min/ session. Per session 30 min computer, 15min table-top.	I: + selective and sustained attention, impulsiveness; = intellectual functioning II: NA III: + adaptive behaviour in the areas of communication, daily livin skills and social skills
Sjö et al., 2009 (41) Moderate	Quasi- experimental pre-/post-test pilot design Pre-post	N = 7 Injury: 3 TBI, 2 BT, 2 Stroke, 10m–8y post-injury Age: 11.3–15.8 y Attention and/ or memory problems.	AMAT-C (see Catroppa et al., 2015) integrated in school.	Setting: 1:1 with child's regular teacher. Duration/frequency: Scheduled:18–20 w, 5 sessions/w, 30–45 min/session Actual: 18–20 w over 6–9 m	I: + verbal and visual memory, cognitive flexibility (on some parameters); = working memory, selective/sustained/divided attention, processing speed, strategy use II: + trainer-reported emotional control, – parent-reported initiation planning/organizing III: NA
Treble- Barna et al., 2015 (38) Weak	Quasi- experimental matched controlled pre-/post-test design Pre-post (18 w after pre)	N = 24 (E:13, C:11) Injury: mild complicated to severe TBI, 1.1– 9.1 y post-injury Age: 9–15 y • Reported attention deficits based on parent rating scale.	AlM: Computerized exercises for attention combined with metacognitive strategies. <i>Control intervention</i> : Healthy controls, no intervention.	Setting: 1:1 meetings with clinician, home practice. Rewards for completing home training sessions. Duration/frequency: Scheduled: 10 w, 1 therapist session/w (60–90min) + 2–4 home sessions/w (20–40 min). Actual: 10–13 therapist sessions, 8–44 home sessions.	l: + sustained attention (some parameters); = selective attention, inhibition, cognitive flexibility, planning ll: + parent-reported executive functioning; = child-reported executive functioning lll: + goal attainment
van 't Hooft et al., 2005/ 2007 (42,43) Strong	Randomized controlled design Pre-post – 6 m	n = 38 (E:18, C:20) Injury: 21 mild to severe TBI, 14 BT, 2 Infection, 1 Anoxia, 1–5 y post-injury Age: 9–16 y • Objectified attention and/or memory problems.	AMAT-C (see Catroppa et al., 2015). Modifications: shorter (17 w), individualized difficulty, rewards, programme overview for children <i>Control intervention</i> : Freely chosen interactive activity with coach.	Setting: 1:1 with parent or teacher as coach at home or at school, 1 meeting per week with clinician, child, and coach at hospital for feedback. Duration/frequency: Scheduled: 17 w, 6 sessions/w, 30 min/session.	I: + visual memory, verbal memory everyday memory, cognitive flexibility, processing speed (all maintained up to follow-up); + sustained and selective attention (on some parameters); + verbal working memory, (not up to follow-up); full scale IQ and verbal inhibition (from pre-test to follow-up) II: NA

^aBased on the Quality Assessment Tool for Quantitative Studies (Effective Public Health Practice Project). ^bWhenever possible, scheduled as well as actual training duration and frequency are displayed. c +: improvement, = : no change, -: deterioration, NA: 'not assessed'. Abbreviations: E = experimental group, C = control group, y = year(s), m = month(s), w = week(s), h = hour(s), min = minutes, M = mean, SD = standard deviation. Abbreviations injury: ABI = acquired brain injury, BT = brain tumour, TBI = traumatic brain injury. Abbreviations interventions: AIM = Attention Improvement and Management, AMAT-C = Amsterdam Memory and Attention Training for Children.

intervention that took place in small groups and lasted 42 hours (stretched over 7 weeks) yielded more positive changes in these areas than shorter 1:1 interventions in these areas. Since only one, although high-quality, study investigated this long (in terms of duration) group-based intervention, it is not clear whether the duration, the setting or the intervention itself (i.e. problem-solving training based on metacognition), underlie the positive effects.



Table 4. Overview of studies into interventions based on external aids, and the combination of external aids and metacognition/strategy use.

Study characteristics		_	Intervention characteristics		Main findings ^c
Authors, quality ^a	Design and measures	Patient characteristics	Intervention	Setting, duration and frequency ^b	I: Cognition on level of functions II: Cognition on level of activities III: Psychosocial and academic outcomes
Ho et al., 2011 (68) Weak	Quasi- experimental pre-/post-test design Pre-post – 3 m	 n = 15 Injury: mild to severe TBI, 1.42–12.25 y post-injury Age: 11–17.42 y Difficulties in everyday memory. 	Self-instruction training combined with diary training and case examples.	Setting: 1:1, 1:2 or 1:3 sessions with instructor, homework assignments regarding diary use and application of skills in daily life. Duration/frequency: Scheduled: 6 w, 1 session/w, 1.5 h/session + regular use of diary + use learned strategies in daily life.	selective attention speed; = verbal memory, sustained attention, sustained divided attention, cognitive flexibility speed, selective attention accuracy II: + parent- and child-reported
Wilson et al., 2009 (67) Weak	Randomized controlled cross- over design – only within- subjects analyses <i>Measures</i> : Pre- Post-5–7 w	n = 12 (E: 4, C: 8) Injury: 5 TBI, 1 Anoxia, 4 Develop-mental problems, 1 Cerebral palsy, 1 Birth injury, 2–3 y post-TBI, 15 y post-birth injury/anoxia Age: 8–17 y • Reported (by therapist) memory and/or planning difficulties.	NeuroPage: reminder messages for individual target behaviours. Diaries were kept regarding (completion of) target behaviours. <i>Control intervention</i> : Keeping diaries regarding target behaviours for measurement purposes.	Setting: Daily life, no therapist contact. Determining target behaviours together with a relative and a researcher at baseline. Duration/frequency: Scheduled: 7 w with pager, individual number of reminders/day (M: 5–23), completing diaries in w6–7 Actual: As scheduled	II: NA II: + number of achieved targets (e.g. doing homework) (maintained up to a 5- to 7-week follow-up) III: NA

^aBased on the Quality Assessment Tool for Quantitative Studies (Effective Public Health Practice Project). ^bWhenever possible, scheduled as well as actual training duration and frequency are displayed. ^c +: improvement, = : no change, -: deterioration, NA: 'not assessed'. *Abbreviations*: E = experimental group, C = control group, y = year(s), w = week(s), h = hour(s), M = mean, SD = standard deviation. *Abbreviations injury*: TBI = traumatic brain injury.

Only one study investigated long-term (i.e. 4-month) effectiveness of the intervention in six children with TBI and found sustained improvements in functional task performance and in performance satisfaction.

Drill-based exercises

Six studies investigated five different cognitive rehabilitation interventions that consisted of drill-based exercises. All interventions were computerized trainings. Participants were groups of n=7 to n=50 patients with TBI, brain tumours, stroke, or a not further specified form of non-TBI ABI. Two studies were randomized controlled trials with active control groups. Four of the interventions were home-based and could be used by the child without supervision. The other two were provided in a 1:1 setting. Intervention duration ranged from approximately 6 hours to approximately 24 hours of training overall (i.e. 50 minutes to 3.5 hours per week) over a period of 5 weeks to 3 months.

Improvements after (computerized) drill-based exercises are mostly seen to the extent that performance improved on the trained tasks or on cognitive tasks similar to the trained tasks in the intervention. In children and adolescents with TBI, the improvement(s) seemed to generalize to enhanced reading abilities in one study with 23 children aged eight to 15 and to parent-rated attention on the long term in another with 12 children aged 12–21. However, these findings require further research since they were only investigated in one study each.

Metacognition/strategy use combined with drill-based exercises

Four interventions combining metacognition and/or strategy use with drill-based exercises were investigated in six different studies with sample sizes ranging from 7 to 65. One was a randomized controlled trial using an active control group; the others were quasi-experimental designs, two of which used a passive control group. Children and adolescents participating in these studies were diagnosed with TBI or various other forms of ABI (i.e. infection, hypoxia, anoxia, birth trauma, brain tumour, or stroke) and were 10 months to 16 years post-injury. The interventions were mostly provided in a 1:1 setting, with a therapist and/or parent practicing with the child. The duration of the interventions ranged from 10 weeks to 6 months with two to seven sessions per week.

Summarizing the results of the six studies, the combination of drill-based exercises with metacognition and/or strategy use training seemed to be effective in enhancing cognitive functioning on the level of functions when examining selective and sustained attention, memory, working memory, and inhibition. This was found in all studies except for one investigating a 10-week attention intervention in 24 children with TBI aged nine to 15. Also, on the level of activities, cognitive functioning improved across multiple studies based on increased parent- or trainer-reported executive functioning and individual goal achievement. Results regarding changes in adaptive behaviour were inconsistent across studies: of the three studies investigating this, two found improvements after the intervention: in one study, this improvement was seen



18 weeks after baseline, in the other study, improvement was found 1 year after baseline, both investigating only children with TBI. The third study that did investigate adaptive behaviour but found no results was a small study of 10 children with various types of ABI (mainly TBI), investigating an 18week attention and memory intervention.

External aids

The use of the external aid NeuroPage as a reminder tool was investigated in one study and was found to be beneficial for everyday memory functioning up to 7 weeks after the intervention in a group of 12 children and adolescents with various forms of ABI. However, the quality of this one study was assessed as weak and results should therefore be interpreted with caution.

Metacognition/strategy use combined with external aids

Combining external aids (i.e. diaries) with metacognition/ strategy use (i.e. self-instruction training) to target memory functioning of 15 children aged 11-17 with TBI seemed to decrease daily memory problems for a short period of time. Cognitive functioning on the level of functions and behavioural functioning improved slightly. The one study that investigated this combination of intervention components was of weak quality.

Discussion

The aim of this systematic review was to provide an up-todate overview of cognitive rehabilitation for children and adolescents with ABI and to compare the effectiveness of different components (i.e. metacognition, drill-based practice, and external aids). Our search yielded 20 articles discussing 19 studies which in total investigated 17 different cognitive rehabilitation interventions. Seven relevant new studies (33-38,53) were found which, to the authors' knowledge, have never been included before in reviews on cognitive rehabilitation for children and adolescents with ABI and therefore add important new knowledge to the limited evidence-base presented in previous reviews.

Summary of evidence

Findings of the current review indicate that the types of components making up a cognitive rehabilitation intervention may play a crucial role in the effectiveness of the intervention. It is important to note that all conclusions of the present review are based on still a limited number of studies that were heterogeneous in multiple important aspects other than intervention components, such as intervention durations settings, but also patient and injury characteristics of the samples included. In the following section, we discuss the evidence for the effectiveness of different intervention types in children with ABI. Furthermore, we consider what effective interventions have in common beyond their components, focussing on intervention variables, such as setting, therapist-involvement, and duration and frequency. Future directions are discussed.

Metacognition/strategy use and the influence of intervention settings

Interventions based on metacognition and/or strategy use seem to have benefits for adaptive behaviour, but less so for cognitive functions, such as memory and executive functions. This is in accordance with previous suggestions that metacognitive skills are essential for promoting behavioural and social functioning of children with ABI (54). While the studies investigating this type of intervention varied greatly regarding study designs and participant characteristics, five of six studies included individual patient-therapist contact. Interestingly, the one intervention that took place in groups yielded even more positive changes (i.e. on more outcome measures) than the individual interventions. Note that in the present review, this effect might be confounded since the group intervention was also the most intensive, providing multiple 3-hour long session over a relatively short period of time. Influence of intervention duration and frequency will be discussed below.

The scarcity of studies into group-treatments included in the present review made it impossible to directly compare their effects to that of 1:1 interventions. However, previous studies have shown that group interventions might provide patients with age-appropriate social experience as well as a relief from social isolation, thereby enhancing the effectiveness of and motivation for the intervention. For example, metacognitive training focused on cooperative learning and social mediation for adolescents with ABI was found to be more effective when provided in a peer-supported context than in a family-based context (32). This is also in line with studies in other populations, indicating for example that a group intervention for adolescents with epilepsy has a positive influence on psychosocial functioning (55,56). For children with ABI, more improvement in cognitive and motor outcomes can be achieved when they receive the intervention in the family context, supported by their parents, than when the intervention was provided directly by a therapist (27). Future studies should investigate further whether family-centred or peer-supported interventions are also feasible in cognitive rehabilitation after paediatric ABI, and whether they have additional benefits compared to 1:1 interventions.

Drill-based/computerized interventions and the effect of intervention duration

Interventions using (computerized) drill-based exercises seem to improve cognitive functions on the level of functions (e.g. verbal working memory in three of the studies, visual spatial working memory in two of the studies and attentional abilities in two of the studies) of children and adolescents with ABI, but only when outcome measures are similar to the training tasks. Improvements in other areas of functioning, such as executive function behaviour or adaptive behaviour, did not consistently occur. These findings are in line with previous studies in other populations such as children with attentiondeficit/hyperactivity disorder (ADHD) and typically developing children (57) and adults with ABI (58), where training of specific functions did not transfer to other function and/or skills. Moreover, in the broader field of cognitive rehabilitation, it has previously been suggested that, to achieve wideranging effects with an intervention, mere repetitive practice

is insufficient and complementary treatments should be employed (59,60).

In the present review, interventions that were based on (computerized) drill-based exercises did not seem to lead to wide-ranging results, but were also the interventions that took place over a relatively short period of time (i.e. 5 weeks to 3 months) with a moderate total training time (i.e. a mean of approximately 11 training hours), while other interventions such as metacognition training and combinations of metacognition and drill-based exercises seem to take longer in general (7 weeks to 10 months and 10 weeks to 6 months respectively) and seem to have a higher total intervention time. The optimal duration, frequency, and total intervention time for any of the intervention types is still unknown: to our knowledge, there is for example no direct comparison between long and short interventions with low or high session frequency. It has previously been suggested that more intensive trainings (i.e. incorporating a large amount of intervention time) will lead to better results in children with ABI (18). In the current review, that suggestion could not be objectively confirmed, because again, heterogeneity in other domains such as patient and injury characteristics made this difficult to investigate. In any regard, these intervention characteristics are important since they may influence selection of a treatment for children with ABI. More specifically, since the effectiveness of cognitive rehabilitation is still not completely clear, treatment choice may be based on costs and time investment (of therapists, but also patients and other persons involved) and thereby indirectly on session duration and frequency.

Metacognition/strategy use combined with drill-based training and target patients

In contrast to the single-component interventions discussed above, multi-component interventions combining metacognition/strategy use training with drill-based training may lead to improvements in a broad range of cognitive functions and psychosocial areas. The results regarding the effectiveness of this combination of interventions are in line with previous literature on the effectiveness of cognitive rehabilitation in other populations. For example, authors of a large-scale review of adult cognitive rehabilitation recommended to combine drill-based attention training with metacognitive training to enhance attention as well as generalization to daily functioning in adults with ABI (59). Similarly, another systematic review indicated that Goal Management Training, a form of metacognitive intervention, in adults with ABI is most efficient when embedded in larger, more holistic programmes (61).

In children with ADHD, a multi-component memory intervention combining memory strategies with memory exercises was found to lead to improvements in memory, attention, and working memory but also parent-rated ADHD behaviour (62). For children and adolescents with ABI, the effects on daily functioning still need to be determined in future research. A recently proposed model specific to the development of intervention for children with ABI also highlights the potential of multi-component interventions, especially if they are sequentially introduced in the intervention, from lower-level process/drill-based training to higherlevel strategy training (63). This model also emphasizes the importance of developmental stage a patient is in. For example, metacognitive trainings may not always be appropriate for young children, since they may not have developed sufficient self-awareness yet to successfully implement the strategies (64). Certain interventions may thus be less effective for children compared to adolescent. This is also highlighted in reviews concerning cognitive interventions for other paediatric patient groups, for example children with ADHD (65). Next to age, many other patient characteristics might influence intervention effectiveness. For example: are interventions more effective for children and adolescents with ABI who have greater impairments in baseline cognitive functioning? Does injury severity or type of injury play a role? The diversity in study designs, samples, and outcome measures of the included studies made it, again, impossible to address these questions in the current review. Of importance for all types of cognitive rehabilitation are also family and environmental factors, such as socio-economic status and family functioning, which have been shown to significantly influence (long-term) outcomes after ABI (28,66). Of the studies included in the present review, only two reported on these factors, making it impossible to further examine their influence on intervention effectiveness across studies. Therefore, further research is required to determine what interventions are optimal for which patients, focusing on type, severity, and time postinjury as well as age of the patients and family environmental factors.

External aids with and without metacognition/strategy use

External aids seemed mainly useful when the treatment goal is to improve specific daily life cognitive functions, such as everyday memory (67). External aids in combination with metacognition/strategy use have additional positive effects on some cognitive functions and limited areas of psychosocial functioning (68), again supporting the use of multi-component interventions. Given that only two studies investigated external aids either alone or in a multi-component intervention, results remain preliminary.

Limitations of the included studies

Many of the available studies have limitations that can affect study results. For one, studies often do not include a control group and randomized controlled trials are rare. Basing conclusions about intervention effectiveness on differences between pre-test and post-test performance without comparison to a control group is prone to biasing influences, such as natural changes in performance over time. Secondly, sample sizes of the included studies are mostly small, potentially leaving them underpowered to detect all but large or very large effects. Thirdly, there is a great variety in outcome measures in the available studies, making a meaningful comparison of results across studies difficult. To make studies more comparable in this regard, a set of common outcome measures should be used, for example recommended by the inter-agency Pediatric TBI Outcomes Workgroup (69).

Most studies included in the present review were rated to be of moderate quality. However, when assessing study

quality, the authors of the present review noted that multiple studies failed to report important information, for example the number of patients approached versus the number of included participants. When this information was not described, the score given for this item was 'moderate', based on the criteria of the quality rating tool (24). Study quality might therefore be under- or over-estimated, due to the lack of information provided in some of the studies. The authors of the present review are aware that performing highquality randomized controlled trials in children with ABI has many challenges, one of which being the necessity to include large samples of participants, due to their heterogeneity with respect to a the great number of factors that could influence intervention effectiveness. Researchers could therefore consider other study designs, such as high-quality single-case experimental designs (SCED) (70-72). Considering SCEDs in the preliminary phase of evidence, as is currently the case with cognitive rehabilitation after paediatric ABI, can help develop randomized controlled trials for promising interventions and even provide some evidence themselves (70-72). Furthermore, SCEDs may also give an indication which factors other than the intervention itself have an influence on the intervention effectiveness. For example, a study investigating metacognitive Goal Management Training in a series of four children with severe ABI found that prospective memory could be improved, but that involvement of parents and teachers is necessary to enhance the intervention effect and achieve generalization to daily life (73).

Limitations of the present review

First, the number of included studies in the present review increased compared to previous reviews (2,15,16,18). Nevertheless, a meta-analysis of the data was not carried out, given that the increase in number of included studies was paralleled by an increase in heterogeneity of outcome measures, patients in terms of age, type, and severity of injury, and investigated interventions differing substantially in aim, duration, and frequency. This large variety in outcomes, patients, and interventions across a relatively small number of studies prevented a meaningful interpretation of meta-analytic statistics. Inconsistent findings in this systematic review might be due to this large variation in patient and intervention characteristics as well as in outcome measures. It is recommended for future studies to further consider these potentially influential factors. Moreover, the problem of large variety in patients and interventions can only be overcome when the amount of studies in this field is increased, enabling better pooling of data.

Second, during the study selection for the present review, four studies were excluded whose sample consisted of children with ABI but also more than 50% children with CNS involving cancer (see inclusion criteria in Methods section and Figure 1). Even though cognitive interventions may be relevant for children with cognitive problems regardless of their diagnosis, previous studies have found that effectiveness is not always the same across different patient groups. For example, the effect of cognitive interventions was found to be larger in children with ABI and neurological disorders than in children with neurodevelopmental disorders such as ADHD (17). Of the excluded studies, two investigated two different computerized drill-based interventions (74,75), while the other two examined the same intervention combining metacognition/strategy use with drill-based attention training (76,77). In line with the conclusions of the present review, effectiveness of the two drill-based intervention mentioned above pertained mainly to cognitive tasks that were similar to the training tasks, except for a short-term improvement (not maintained over 3 months) in parent-reported learning problems (74). The two studies investigating the multicomponent intervention found improvements in the area of attention as well as on academic achievement measures (76,77); this again is in line with the conclusions of the present review, indicated the potential of multi-component interventions to improve different areas of functioning. Contrarily, in the present review, five studies were included that investigated not only children with ABI (more than 50% of the sample) but also children with other disorders that affected their cognitive functioning, such as CNS involving cancer and epilepsy. Excluding these five studies would weaken our review to the extent that the conclusions would be based on a smaller number of studies, but the conclusions itself would not change. Including the four studies that did not meet the criterion would, similarly, not change the conclusions of the present review. Moreover, rather than strengthening the conclusions because of the increased number of studies, including these studies would have introduced equivocality of the results regarding effectiveness of cognitive interventions for children with ABI, given the high number of children who did not suffer from ABI.

Third, four of the articles found in the database search did not have an abstract and/or full text available online. These articles (published between 1972 and 1989) were also not described in any of the previous reviews investigating cognitive rehabilitation for children and adolescents with ABI, and they were all published in national (i.e. German and South African) journals.

Lastly, of the 20 articles included in the present review, only 13 were derived from the database search and e-mail alerts following that search. This suggests that not all articles are consistently based on the same system, emphasizing the importance also of expert selection of relevant studies. Thanks to the large expert network and the thorough search of reference lists of included articles and previous reviews, we are confident that all relevant articles meeting inclusion criteria for the present review were recovered.

Conclusions

The present review was the first to specifically focus on components of cognitive rehabilitation when investigating their effectiveness in improving cognitive functions (e.g. attention, memory and executive functions) in children and adolescents with ABI. In the current review, 17 different cognitive rehabilitation interventions were examined. Results suggest that multi-component interventions combining for example metacognition/strategy use with (computerized) drill-based exercises seems to have potential to improve cognitive functioning on the level of functions and activities, as well as daily life functioning of children and adolescents with ABI. Although intervention, patient and outcome heterogeneity in the present review make definite conclusions difficult,



findings from previous studies suggest that, in addition to being of a multi-component nature, cognitive (rehabilitation) interventions are most promising when they are intensive, appropriate for the developmental stage of the child, and provided in a family- or peer-supported context.

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